Proposed claims for Serial No. 09/806,368 (our ref: 2923-581):

1. (Canceled) ~~A mature protein having an antagonistic activity against bone morphogenetic proteins, obtained by converting at least one methionine or tryptophane residue existing in the receptor binding site of mature human MP52 (SEQ ID NO 1) to a hydrophilic residue by chemical modification, or replacing said residues with a hydrophilic amino acid residue or a polar amino acid residue.~~

2. (Currently Amended) The mature modified protein according to claim 16, wherein the chemical modification for said methionine residue is an oxidization reaction.

3. (Currently Amended) The mature modified protein according to claim 2 in which four methionine residues are oxidized and having the amino acid sequence of SEQ ID NO 5.

4. (Currently Amended) The mature modified protein according to claim 16, wherein the chemical modification for said methionine residue is an alkylation reaction.

5. (Currently Amended) The mature modified protein according to claim 4 wherein the alkylation reaction is S-carboxymethylation in which at least one methionine residue is S-carboxymethylated and having the amino acid sequence of SEQ ID NO 6.

6. (Currently Amended) The mature modified protein according to claim 16, wherein the chemical modification for said tryptophane residue is an allylsulphenylation reaction.

7. (Currently Amended) The mature modified protein according to claim 6 in which two tryptophane residues are allylsulphenylated and having the amino acid sequence of SEQ ID NO 7.

8. (Currently Amended) The mature modified protein according to claim 16, wherein said mature human MP52 is a dimer protein.

9. (Currently Amended) A mature protein ~~having an antagonistic activity against bone morphogenetic proteins,~~ obtained by converting at least one residue of tryptophane residues existing in the amino acid sequences of mature human BMP-2 (SEQ ID NO 2), mature human BMP-4 (SEQ ID NO 3) or mature human BMP-7 (SEQ ID NO 4) to a hydrophilic residue by chemical modification, or replacing said residues with a hydrophilic amino acid residue or a polar amino acid residue.

10. (Currently Amended) A mature protein ~~having an antagonistic activity against bone morphogenetic proteins,~~ obtained by replacing at least one amino acid residue of three hydrophobic amino acid residues, among said hydrophobic amino acid residues relating to a receptor binding site in the amino acid sequences of mature human BMP-2 (SEQ ID NO 2), mature human BMP-4 (SEQ ID NO 3), or mature human BMP-7 (SEQ ID NO 4), which are located in positions corresponding to those of methionine residues located in 30th, 71st, and 74th positions of the amino acid sequence of mature human MP52 (SEQ ID NO 1) with a hydrophilic amino acid residue or a polar amino acid residue.

11. (Previously Presented) The mature protein according to claim 9, wherein said mature human BMP-2, mature human BMP-4, or mature human BMP-7 is a dimer protein.

12. (Currently Amended) An agent for therapy and/or prevention of symptoms of ectopic ossification which occurs along with increased BMP expression ~~is related to~~

~~BMPs~~, containing a mature protein according to claim 16 as an effective ingredient showing an antagonistic activity against a bone morphogenetic protein.

13. (Currently Amended) An agent for therapy and/or prevention of symptoms of calcification assoc. w/ metab. dis. metabolic diseases with calcification wherein said disease occurs along with increased BMP expression ~~is related to the expression of BMPs~~, containing a mature protein according to claim 16 as an effective ingredient showing an antagonistic activity against a bone morphogenetic protein.

14. (Currently Amended) A method of treating ectopic ossification which occurs along with increased BMP expression ~~is related to BMPs~~, in warm-blooded animals comprising administering to warm-blooded animals in need thereof an amount of a mature protein according to claim 16 sufficient to treat ectopic ossification.

15. (Currently Amended) A method of treating metabolic diseases with calcification wherein said diseases occur along with increased BMP expression ~~are related to the expression of BMPs~~, in warm-blooded animals comprising administering to warm-blooded animals in need thereof an amount of a mature protein of claim 16 sufficient to treat said metabolic diseases.

16. (Previously presented) A mature modified protein obtained by converting at least one methionine or tryptophan residue existing in the receptor binding site of mature human MP52 (SEQ ID NO:1) to a hydrophilic residue by chemical modification, or replacing said residues with a hydrophilic amino acid residue or a polar amino acid residue. Functional limitation

17. (Canceled) ~~A mature protein having a BMP antagonist-like activity obtained by converting at least one methionine or tryptophan residue existing in the~~

~~receptor binding site of mature human MP52 (SEQ ID NO:1) to a hydrophilic residue by chemical modification, or replacing said residues with a hydrophilic amino acid residue or a polar amino acid residue.~~

18. (Previously presented) A mature modified protein obtained by converting at least one methionine residue at position 30, 71 or 74 or at least one tryptophan residue existing in mature human MP52 (SEQ ID NO:1) to a hydrophilic residue by chemical modification, or replacing said residues with a hydrophilic amino acid residue or a polar amino acid residue, wherein said mature modified protein has antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7.

19. (Currently amended) A mature, modified protein ~~having an antagonistic activity against bone morphogenetic proteins,~~ obtained by converting at least one methionine or tryptophane residue existing in the receptor binding site of mature human MP52 (SEQ ID NO 1) to a hydrophilic residue by chemical modification, or replacing said residues with a hydrophilic amino acid residue or a polar amino acid residue, wherein said mature modified protein has antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7.

affection w/a dis due to ectopic.

20. (New) A method for treating a disease which is due to ectopic expression of BMPs in warm-blooded animals comprising administering to warm-blooded animals in need thereof an effective amount of a mature modified protein according to claim 16.

Alternative claims 12-15

12. (Currently Amended) An agent for therapy ~~and/or prevention of symptoms of ectopic ossification which is related to BMPs,~~ containing a mature modified protein according to claim 16 ~~as an effective ingredient showing an antagonistic activity against a bone morphogenetic protein~~.

13. (Currently Amended) An agent for therapy of diseases due ~~and/or prevention of symptoms of metabolic diseases with calcification wherein said disease is related~~ to the expression of BMPs, containing a mature modified protein according to claim 16 as an effective ingredient, wherein said mature modified protein has antagonistic activity against at least one BMP protein selected from the group consisting of MP52, BMP-2, BMP-4 and BMP-7 ~~showing an antagonistic activity against a bone morphogenetic protein~~.

14. (Currently Amended) A method of treating ectopic ossification which is due to ectopic expression of BMPs, ~~is related to BMPs~~, in warm-blooded animals comprising administering to warm-blooded animals in need thereof an amount of a mature modified protein according to claim 16 sufficient to treat ectopic ossification.

15. (Currently Amended) A method of treating calcification of arterial sclerosis ~~metabolic diseases with calcification wherein said are related to the expression of BMPs~~, in warm-blooded animals comprising administering to warm-blooded animals in need thereof an amount of a mature modified protein of claim 16 sufficient to treat said calcification of arterial sclerosis ~~metabolic diseases~~.